

## REMARKS

In an Office Action mailed August 7, 2009, the Examiner in charge of the application correctly stated the status of the claims. Claims 2, 3, 14, and 15 have been cancelled; Claims 1, 4-12, 25, and 28 are withdrawn from consideration as being drawn to non-elected subject matter; and Claims 13, 16-24, 26, and 27 are under consideration. The Examiner maintained that the claimed invention is obvious over Russell *et al.* in view of Xu *et al.* Applicants respectfully traverse the rejection below.

### **Rejection under 35 U.S.C. § 103**

Claims 13, 16-24, 26, and 27 are rejected for alleged obviousness over Russell in view of Xu. According to the Examiner, Russell teaches an hES cell culture composition (Office Action, page 4, fifth paragraph), including an apparatus, and Xu teaches growing hES cells without feeder layers. Applicants submit that the skilled artisan reading Russell would not have found it obvious to use the apparatus to maintain undifferentiated, proliferating hES cells by applying strain. To the extent that Russell teaches anything about employing hES cells, one skilled in the art would have expected that growing hES in the apparatus would accelerate, rather than inhibit, differentiation because Russell's apparatus membrane "provides enhanced cellular differentiation" (Russell, paragraph [0009]) of myocytes. The Examiner failed to explain why it would be obvious to use the Russell apparatus that enhances differentiation of myocytes to prevent differentiation of hES cells cultured in the apparatus.

The Examiner emphasized that "Russell teaches a method to maintain a differentiated in vivo cell phenotype" (Office Action, page 2, last paragraph). It is unclear how maintaining differentiation would have made obvious to one of skill in the art Applicants' cell culture composition of undifferentiated human ES cells. The Examiner further noted that "Russell is not about to 'differentiate' undifferentiated precursor or stem cells to differentiated cells" (Office Action, page 2, last paragraph). Even assuming, arguendo, that Russell does not teach that its apparatus membrane "provides enhanced cellular differentiation" (which, of course, it does, *see* Russell, paragraph [0009]), maintaining differentiated cells does not make obvious perpetuating stem cells in a pluripotent state. Terminally differentiated cells, such as fibroblasts, are programmed to remain differentiated. Absent elaborate reprogramming techniques, terminally differentiated cells, such as those taught by Russell, do not dedifferentiate. Thus, maintaining

cells in a differentiated state means no more than keeping them alive. Embryonic stem cells, however, require elaborate conditions to remain in an undifferentiated, pluripotent state. Maintaining differentiated cells in a differentiated state cannot make obvious preventing stem cells from differentiating.

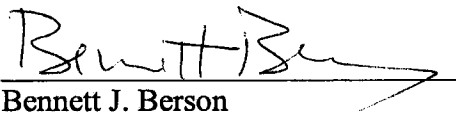
The Examiner alleged that "ES cells before or after [strain] application ... should be the same" (Office Action, page 4, first paragraph). However, Applicants demonstrated that embryonic stem cells remain undifferentiated when subjected to stretching but undergo spontaneous differentiation without stretching (e.g., specification, paragraphs [0029]-[0030]). Consequently, the cells are not the same. If, as the Examiner alleged, strain application has no effect on ES cells, then the Examiner failed to explain why one of skill in the art would have been motivated to grow human ES cells in Russell's apparatus and apply strain.

The Examiner's allegation that applying strain has no effect on ES cells would eliminate any motivation for the skilled artisan to combine Russell with Xu, which describes a feeder-free human embryonic stem cell culture. Applicants reiterate that a combination of Russell and Xu was in any event not obvious because it would have required the skilled artisan to ignore Russell's teaching that cell differentiation is accelerated in response to applying strain. Reconsideration is respectfully requested.

Fees

A Petition for an extension of time for two months accompanies this Response so the Response will be deemed to have been timely filed. Please charge the fee due to the Deposit Account 17-0055. No other fee is believed due in connection with this submission. If a fee is due, in this or any subsequent response, please charge the fee to the same Deposit Account.

Respectfully submitted,



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